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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,678	06/04/2003	Francesco Tato	4161-2	4826

23117 7590 11/25/2005

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EXAMINER	
GRAFFEO, MICHEL	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 11/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,678	TATO ET AL.	
	Examiner	Art Unit	
	Michel Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-67,71 and 72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-32, 35-44, 47-67 and 71-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

Claims 28-67 and 71-71 are pending and examined.

In response to the Office Action dated July 6, 2005, Applicant amended claims 60-61, cancelled claims 68-70 and added new claims 71-72.

Applicant's arguments, see Amendment, filed October 6, 2005, with respect to the rejection made under 35 U.S.C. 112 to claims 68-70 have been fully considered and are persuasive. The rejection of claims 68-70 with respect to 35 U.S.C. 112 has been withdrawn. Applicant's arguments with respect to the rejection made under 35 U.S.C. 103 with respect to claims 33-34 and 45-46 has been considered and is persuasive. The rejection made under 35 U.S.C. 103 with respect to claims 33-34 and 45-46 is withdrawn. Any rejection not specifically stated in this Office Action has been withdrawn.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made

> to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28-32, 35-44, 47-67 and 71-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0297946 to Fondy et al. in view of Richman et al. Interferon Protects Normal Human Granulocyte/Macrophage Colon-Forming Cells from Ara-C Cytotoxicity. Journal of Biological Response Modifiers. 570-575 (1990), taken together with WO94/12202 to University of Dundee.

Fondy et al. teach a method of treating cells in vivo (see page 4 lines 35-37) and in vitro (see page 4 lines 43-47) comprising a protective cytochalasin compound such as cytochalasin D (see page 4 lines 25-30) and an antineoplastic agent such as the vinca alkaloids (see page 7 lines 17-24) wherein the components can be administered sequentially (see page 4 lines 48-50).

Fondy et al. state that the cytochalasin and antineoplastic agents can be administered sequentially but do not recite specific examples thereto. As applied below, Richman et al. teach a method of treating normal and malignant cells in vitro comprising a 1 hr pretreatment of a protective compound.

Richman et al. teach a method of treating normal and malignant cells in vitro comprising a 1 hr pretreatment (see Summary) of a protective compound, specifically IFN which is known to block cell cycle progression in normal cells (see introduction page 570), followed by a treatment with Ara-C (cytarabine) resulting in the protection of normal cells (see Results page 572) whereas there is no significant protection of leukemia cells (see Results page 573).

Neither Fondy et al. nor Richman et al. speak directly about tumor cells having an inactive p53 pathway. Nonetheless, Applicant admits on page 5 lines 1-5 of the specification that most tumor cells lack a functional p53 pathway. Additionally, University is cited to show the state of the art at the time the instant application was filed and teaches that mutation of p53 is a very common genetic alteration in human cancers (see page 1 in the background of the invention). Thus these claims would be appropriate for almost any tumor model.

Neither Fondy et al. nor Richman et al. recite the treatment of alopecia specifically, but since alopecia is caused by chemotherapies that are not selective for normal proliferating cells, one skilled in the art would find the treatment of alopecia to be a necessary result of the claimed invention.

Neither Fondy et al. nor Richman et al. teach specific times for multiple rounds of pretreatments and treatments with the claimed method. Nonetheless, one skilled in the art would find it obvious in view of routine optimization to vary the times for pretreatment and washing of the cells in preparation for an additional round of pretreatment and treatment.

One skilled in the art would be motivated to combine Fondy et al. with Richman et al. Both are directed to the specific protection of non-cancerous cells by inhibiting cell cycle progression while targeting proliferating tumor cells. Further, Richman et al. suggest that the protective agent and chemotherapy can be administered sequentially as well as concurrently (see Examples 16 and 17 which show in vitro treatment of cells with ADR which were treated with cytochalasin according to Example 14). Thus, the claimed invention of the composition was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Response to Arguments

Applicant's arguments filed October 6, 2005 have been fully considered but they are not persuasive. As Applicant points out, Fondy teaches the administration of the chemotherapeutic agent from 5 to 30 minutes prior to administration of a cytochalasin. Although this time frame is not coextensive with that recited in claims 33-34 or 45-46, it is with respect to for example claim 28, which recites that the pretreatment with the protective compound is carried out before the treatment with the chemotherapeutic

agent. Absent any specificity to the treatment regime, Fondy provides a prior teaching of such claimed limitation. Similarly, Richman teaches a pretreatment of a protective compound for an hour and again Applicant's arguments are unpersuasive since the claims, such as independent claim 28, do not recite any specific range of time between treatments with the protective compound and the chemotherapeutic agent.

Having noted that both Fondy and Richman teach a pretreatment of a particular length of time one of ordinary skill in the art would have made the connection between the cell cycle arrest taught in Richman and the teaching in Fondy that cytochalasins are known to alter microfilament morphology (similarly to the mechanisms of other chemotherapeutic agents that have been traditionally used to combat cancer such as those that break down tubulin). And to that extent, one of ordinary skill in the art would have had an expectation of success to combine Fondy and Richman.

Although Richman may not have appreciated the p53 dependency of the cell cycle arrest, Richman provides an explanation for the cell cycle arrest necessarily present in Fondy (necessarily present since the compounds administered in Fondy are the same as those in the instant claims since products of identical chemical composition can not have mutually exclusive properties. In other words, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present). Lane then adds to Richman the knowledge that the p53 pathway is involved in cell cycle arrest and that the mutants described therein result in an inactive p53 pathway (see especially the Abstract).

Conclusion

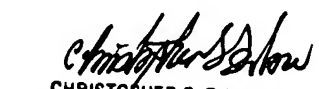
Claims 28-32, 35-44, 47-67 and 71-72 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

15 November 2005
MG